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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,280	05/27/2005	Jane Sanders	AATH.P-001	1845

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EXAMINER
WOODWARD, CHERIE MICHELLE

ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
06/02/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,280	SANDERS ET AL.	
	Examiner	Art Unit	
	Cherie M. Woodward	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *157-159,162-171,173-179 and 182-195* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *121,122,126,127,129,130,133,136, 137,198 and 200-203* is/are rejected.

7)☒ Claim(s) *134 and 135* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 May 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 121,122126,127,129,130,133-137,157-159,162-171,173-179,182-195,198, and 200-203.

DETAILED ACTION

Formal Matters

1. Applicant's Response filed 3/12/2009 is acknowledged and entered. Claims 1-120, 123-125, 128, 131, 132, 138-156, 160, 161, 172, 180, 181, 196, 197, and 199 have been cancelled by Applicant. New claims 200-203 have been added. Claims 157-159, 162-171, 173-179, and 182-195 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 121, 122, 126, 127, 129, 130, 133-137, 198, and 200-203 are under examination.

Advisory Notice

2. With regard to Applicant's comments on page 15 of the remarks, rejoinder under lack of unity will be considered by the examiner when the claims under examination are in condition for allowance. At present, the claims under examination are not allowable. The examiner notes that Applicant has marked the status identifier of withdrawn claim 168 as "currently amended." This is an improper status identifier for a withdrawn claim. The status identifier should read "withdrawn, currently amended." Applicant's representative may not withdraw or rejoin claims from/under examination. That is the examiner's responsibility. Appropriate correction is required.

Response to Arguments

Objections/Rejections Withdrawn

3. The objection to the drawings is withdrawn. The examiner thanks Applicant's representative for pointing out the preliminary amendments to the drawings with Replacement Sheets, filed on 5/27/2005.

4. The objection to the disclosure is withdrawn. The examiner thanks Applicant's representative for pointing out the preliminary amendments to the specification filed on 5/27/2005.

5. Rejections drawn to claims 125, 128, 131, 132, and 199 are moot in light of Applicant's cancellation of these claims.

6. The rejection of claims 121 and 122 under 35 U.S.C. 102(b) as being anticipated by Akamizu et al., (Endocrinology. 1999 Apr;140(4):1594-1601), is withdrawn in light of Applicant's amendments and in light of the Declaration of inventor Rees Smith, filed 3/12/2009.

7. The rejection of claims 121, 122, 126, 127, 129, 130, and 133 under 35 U.S.C. 102(b) as being anticipated by Kohn et al., (J Clin Endo and Metab. 1997;82(12):3998-4009) is withdrawn in light of Applicant's amendments and in light of the Declaration of inventor Rees Smith, filed 3/12/2009.

Claim Rejections/Objections Maintained

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 121 and 122 remain rejected under 35 U.S.C. 102(b) as being anticipated by WO 91/09137 (published 27 June 1991, cited in Applicant's IDS of 7/20/2005), for the reasons of record and the reasons set forth herein.

Applicant argues repeats previous arguments that the '137 publication does not teach isolated and/or purified human monoclonal antibodies (Remarks, p. 14). Applicant argues that the characteristics of inhibition of TSH binding to the TSH receptor and stimulation of cAMP by cells expressing the TSH receptor by the antibodies of the '137 publication could be separate components from the polyclonal mixture (Remarks, p. 14).

Applicant's argument has been fully considered, but it is not persuasive. The human monoclonal antibodies taught by the '137 publication are not recombinant antibodies, but they are purified, meeting the limitations of claims in the alternative (see pages 36-42, especially p. 39). As previously stated of record, human polyclonal sera can functionally act as monoclonal preparations (see, for example, Saper et al., previously cited of record, especially at p. 162, column 1, first full paragraph). Further, polyclonal sera are comprised of a multiplicity of monoclonal antibodies each directed to specific antigenic epitopes.

Absent evidence to the contrary, the antibodies taught by the '137 publication meet the limitations of the claims. Because the Patent Office does not have the facilities to determine whether the antibodies of the '137 publication comprise the characteristics of inhibition of TSH binding to the TSH receptor and stimulation of cAMP by cells expressing in the same or different monoclonal antibodies comprising the polyclonal serum, the burden is on the application to show a novel and unobvious difference between the claimed binding partners/antibodies those of the prior art. See In re Brown, 59 CCPA 1036, 459 F.2d. 531, 173 USPQ 685 (CCPA 1972) (holding at 1041, "[a]s a practical matter, the

Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith") and Ex parte Gray, 10 USPQ 2d 1922, 1924-25 (PTO Bd. Pat. App. & Int.).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 121, 122, 126, 127, 129, 130, 133, 136 and 137 remain rejected and claim 198 is also rejected under 35 U.S.C. 103(a) as being unpatentable over WO 91/09137 (published 27 June 1991) and Van Der Heijden et al., (Clin Exp Immunol. 1999;118:205-212), as evidenced by UniProt, Accession No. P16473 (sequence version 1, 1 August 1990), Harlow et al., Eds. (Antibodies, A Laboratory Manual. Cold Spring Harbor Press. 1988, and Kohn et al., (J Clin Endo and Metab. 1997;82(12):3998-4009), for the reasons of record and the reasons set forth herein.

Applicant argues that the claimed antibodies do not fall within the limitations of the present claims (Remarks, p. 14). Applicant's argument has been fully considered, but it is not persuasive.

This rejection was previously presented. However, it has been reformulated in light of Applicant's amendments. Additionally, Applicant is reminded that the order of references in a rejection under 35 USC 103(a) is immaterial. *In re Albrecht and Fleming*, 579 F.2d 92, 198 USPQ 208 (CCPA 1978). It is also noted that the scope of claim 198 has changed based on the change in scope of independent claim 121. It is noted that the limitations of cancelled claim 131 are incorporated into claim 121. However, claim 198 was not dependent on claim 131, but rather only on claim 121. Because of Applicant's amendments, the scope of independent claim 121 has been changed, making the rejection of claim 198 necessitated by amendment.

The Examiner finds the following facts:

a. WO 91/09137 teaches purified binding partners for a TSH receptor comprising monoclonal antibodies, which are found in polyclonal sera (pages 36-42, especially p. 39). Example VIII teaches human autoantibodies in the serum of patients with autoimmune thyroid disease (pp. 101-113). Example VIII teaches human autoantibodies against the TSH receptor in Graves' disease and Hashimoto's thyroiditis (p. 101, lines 7-11). These human autoantibodies are taught as capable of interacting with the TSH receptor and of either mimicking the action of TSH in leading to thyroid hyperfunction or of blocking TSH action with consequent hypothyroidism (p. 101, lines 11-15). The physical characteristics/properties of the autoantibodies include interacting with the TSHR (compare instant claims 121 and 122) and competing with TSH for binding to TSHR (compare instant claim 121), as well as antibodies that induce cAMP production in thyroid cells (compare instant claims 121 and 122).

b. The '137 publication does not teach fragments of human monoclonal antibodies with the requisite characteristics.

c. Van Der Heijden et al., teach fragments of human monoclonal phage antibodies (moPhabs) generated by phage display reactive with the TSH receptor (abstract). Cloning and expression of modified human scFv proteins is taught at p. 207, column 1, paragraph 3 (see also p. 208, column 1, first full paragraph). Expression and purification of scFv fragments are taught at p. 207, column 1, last paragraph. Binding of the moPhabs to the TSHR ectodomain is taught at Figure 1, p. 209. Monovalent and bivalent scFv fragments were tested in a cAMP assay for their modulating effect on TSH-R function (p. 209, column 2, last paragraph) (compare instant claims 136 and 137).

d. The amino acid sequence of human TSHR was well known in the art at the time of the instant invention, as evidenced by UniProt, Accession No. P16473 (sequence version 1, 1 August 1990).

e. The production of monoclonal antibodies via hybridomas, or through recombinant techniques, including fragments thereof is has been routine in the art since at least 1988, as evidenced by Harlow et al., Eds. (Antibodies, A Laboratory Manual. Cold Spring Harbor Press. 1988).

f. Kohn et al., provide evidence of routine tests for cAMP activity, TSH binding to the TSH receptor, and binding affinity to the TSHR (abstract; Figure 1; p. 3999, column 2, last paragraph to p. 4000, column 1, first paragraph; p. 4000, column 2, fourth paragraph; p. 3998, column 2, last paragraph; Table 1, p. 4002; Figure 2, p. 4003; Table 2, p. 4004; Figure 3, p. 4004; Table 4, p. 4006; and Figure 5, p. 4006). Percent inhibition is also shown in a commercial TRAK assay in Table 3 (p. 4005) and Figure 4.

g. As previously stated of record, human polyclonal sera can functionally act as monoclonal preparations. Further, polyclonal sera are comprised of a multiplicity of monoclonal antibodies each directed to specific antigenic epitopes.

h. A person of ordinary skill in the art at the time the invention was made would have reasonably known that fragments of human monoclonal antibodies could be purified from or made against a known antigen or antigenic sequence, such as the TSHR.

i. Further, a person of ordinary skill in the art would have been able to make fragments of human monoclonal antibodies or human recombinant antibodies merely by using well-known methodologies and protocols, such as the ones taught by the '137 publication or Van Der Heijden et al., and the resulting structure and function of the constructs would have reasonably been predictable.

j. There was a recognized need in the art at the time the invention was made to find human antibodies that can be practically and cost-effectively used as diagnostics and as immunotherapetuics for thyroid-based autoimmune disorders such as Graves' disease and Hashimoto's thyroiditis (see WO 91/09137, p. 3, line 25-33, p. 4, lines 31-34, and p. 5, lines 26-34).

k. At the time of the instant invention, there were a finite number of identified predictable potential solutions recognized in the art to solve the problem making find human antibodies that

can be practically and cost-effectively used as diagnostics and as immunotherapetuics for thyroid-based autoimmune disorders such as Graves' disease and Hashimoto's thyroiditis.

l. One of ordinary skill in the art could have pursued the known potential solutions with a reasonable expectation of success to generate human monoclonal antibodies, human recombinant antibodies or fragments of human monoclonal antibodies with a reasonable expectation of success because the art teaches the generation of these antibodies with varying degrees of functional activities.

m. A person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance, the fact that a combination was obvious to try might show that it was obvious under 35 USC 103 (see KSR v. Teleflex, 550 US 389, 421, 82 USPQ2d 1385, 1397 (S.Ct. 2007).

In view of the facts recited above, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the prior art elements according to known methods to yield predictable results or alternatively it would have been obvious to try given the teachings of the prior art. The production of monoclonal antibodies via hybridomas, including the production of antibody fragments has been routine in the art since at least 1988, as evidenced by Harlow et al., Eds. One of skill in the art would have recognized that the results of the combination of functional, active human monoclonal antibodies or fragments thereof, as taught by the '137 publication and Van Der Heijden, would be useful in a commercial and clinical setting and would have been motivated at least to try to purify/isolate human monoclonal antibodies and/or fragments thereof from polyclonal sera with the requisite activity levels in order to treat or diagnose thyroid-based autoimmune disease. Human polyclonal sera can functionally act as monoclonal preparations. Further, polyclonal sera are comprised of a multiplicity of monoclonal antibodies each directed to specific antigenic epitopes.

A person of ordinary skill in the art at the time the invention was made would have reasonably known that fragments of human monoclonal antibodies could be purified from or made against a known antigen or antigenic sequence, such as the TSHR. The '137 publication provides the starting material and Van Der Heijden provides the methodology for producing fragments. Moreover, antibody characterization, functional activity testing, and binding affinity tests are old and routinely used in the art, as evidenced by Harlow et al., and Kohn et al.

The '137 publication teaches that there was a recognized need in the art at the time the invention was made to find human antibodies that can be practically and cost-effectively used as diagnostics and as immunotherapetuics for thyroid-based autoimmune disorders such as Graves' disease and Hashimoto's thyroiditis. The known need in the art for diagnostic tests, methods of treatment, and competition assays using binding partners of the TSHR with the requisite characteristics would have been sufficient to provide the motivation and rationale to try, as taught by the '137 publication. One of skill in the art would have had a reasonable expectation of success because purified TSHR binding partners/antibodies were well known in the art, as taught by the '137 publication, the sequence of the TSHR was known in the art, as evidenced by UniProt, Accession No. P16473, methods of making human monoclonal and recombinant antibodies and fragments thereof were old and routine in the art, as evidenced by Harlow et al., Eds,. and routine screening, activity, and binding affinity tests were also well known in the art, as evidenced by Kohn et al. Further, it is old and well known in the art polyclonal sera are comprised of a multiplicity of monoclonal antibodies each directed to specific antigenic epitopes. It is old and well known in the art that different antibody clones can have different activity levels depending on the epitope to which they bind. The sequence of the TSHR was known in the art, as evidenced by UniProt, Accession No. P16473. The skilled artisan could have reasonably and predictably used the purified TSHR binding partners taught by the '137 publication to isolated monoclonal antibodies from the polyclonal sera that had the claimed characteristics including, inhibitory activity levels, cAMP stimulatory activity levels, and binding affinities.

Absent evidence to the contrary, the antibodies taught by the '137 publication meet the limitations of the claims. Because the Patent Office does not have the facilities to determine whether the antibodies of the '137 publication comprise the characteristics of inhibition of TSH binding to the TSH receptor and stimulation of cAMP by cells expressing in the same or different monoclonal antibodies comprising the polyclonal serum, the burden is on the application to show a novel and unobvious difference between the claimed binding partners/antibodies those of the prior art. See *In re Brown*, 59 CCPA 1036, 459 F.2d. 531, 173 USPQ 685 (CCPA 1972) (holding at 1041, "[a]s a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith") and *Ex parte Gray*, 10 USPQ 2d 1922, 1924-25 (PTO Bd. Pat. App. & Int.).

Additionally, with regard to the inhibitory activity and affinity levels of claims 126, 127, 129, 130, 133, 136, 137, and 198, the Patent Office does not have the facilities to comparatively test the human anti-TSHR monoclonal antibodies taught by the art for the requisite comparative NIBSC units of activity

or binding affinity. Absent evidence to the contrary, the burden is on the application to show a novel and unobvious difference between the claimed TSHR binding partners activity and affinity levels and those of the prior art. See *In re Brown*, 59 CCPA 1036, 459 F.2d. 531, 173 USPQ 685 (CCPA 1972) (holding at 1041, "[a]s a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith") and *Ex parte Gray*, 10 USPQ 2d 1922, 1924-25 (PTO Bd. Pat. App. & Int.).

New Claim Objections/Rejections

Claim Rejections - 35 USC § 101, Product of Nature

14. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

15. New claims 200-203 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims, as written, read on products of nature that are not isolated or purified. The "binding partners" of claims 200-203 encompass naturally occurring human autoantibodies. Not all naturally occurring antibodies/binding partners have been sequenced, so the SEQ ID limitations in the claims are insufficient to overcome a product of nature rejection absent a showing that the claimed binding partners are not, in fact, found in nature. Moreover, with respect to claim 202, the examiner previously noted of record that

In order to overcome this rejection, Applicant should amend the claims to recite that the antibodies are isolated and/or purified.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. New claim 202 is rejected under 35 U.S.C. 102(b) as being anticipated by Hoogemboom et al., US Patent 5,565,332 (15 October 1996)

The '332 patent teaches antibodies/binding partners comprising SEQ ID NO: 115 (residues 31-35) which are 100% identical SEQ ID NO: 2. See also, search results in SCORE.

Provisional Obviousness-Type Double Patenting Rejection

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 121, 122, 126, 127, 129, 130, 133, 136, 137, and 198 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 63-66, and 70 of copending Application No. 12/333,741. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to binding partners, including monoclonal antibodies, recombinant antibodies, and fragments thereof, for a TSH receptor wherein the binding partner has stimulating activity and competes for binding with to the TSH receptor. Absent evidence to the contrary and given the teachings in the specification of the '741 publication, the binding partners of the '741 application are the same binding partners claimed in the instant application.

Applicant is reminded that MPEP § 804 (II) states, "When considering whether the invention defined in a claim of an application would have been an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. *General Foods Corp. v.*

Studiengesellschaft Kohle mbH, 972 F.2d 1272, 1279, 23 USPQ2d 1839, 1846 (Fed. Cir. 1992). This does not mean that one is precluded from all use of the patent disclosure." (Emphasis added). "Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. *In re Vogel*, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970)."Claims 51, 53-55, 57, 59-61, 63, and 65 are provisionally rejected on the ground of nonstatutory double patenting over claims 59, 61, 62-70, 75, 77-79, 71, 73 of copending Application No. 11/775,189. This is a provisional double patenting rejection since the conflicting claims have not yet been patented. The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: The claims are drawn to the same subject matter, being a method of improving the outcome of a spinal surgery procedure in a subject comprising administering a TNF inhibitor wherein the TNF inhibitor is an antibody or antibody fragment. The claims of the instant application are drawn to the same subject matter of the '189 application and render obvious and are rendered obvious by the co-pending application.

Applicant is reminded that Applicant must respond to this rejection even though the rejection may be traversed (see 37 CFR 1.111(b) and MPEP 714.02). Applicant is also referred to *In re Baselle Poliolefine Italia*, 2007-1450, slip op. at 13 (Fed. Cir. 13 Nov 2008).

The examiner notes that the '741 application was filed on 12/12/2008, after the date of the last Office Action, accordingly, the rejection could not have previously been made.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Allowable Subject Matter

20. Claims 134 and 135 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Claims 121, 122, 126, 127, 129, 130, 133, 136, 137, 198, and 200-203 are rejected.
Claims 134 and 135 are objected to.

21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cherie M. Woodward whose telephone number is (571)272-3329. The examiner can normally be reached on Monday - Friday 9:30am-6:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cherie M. Woodward/
Primary Examiner, Art Unit 1647